CLAIMS

What is claimed is:

1. A method of forming a cross-linked coating on a medical device, comprising the steps of:

(a) immersing the medical device in a first solution comprising an organic solvent and a multifunctional crosslinking agent; and

(b) immersing the medical device in a second solution comprising an organic solvent and a cross-linkable biomolecule.

2. The method of claim 1, wherein prior to immersing the medical device in the first solution or second solution as provided in steps (a) and (b), the medical device is immersed in a wetting solution.

3. The method of claim 1 wherein the first solution does not comprise water and the second solution comprises from about 10 to 80 percent water by volume.

4. The method of claim 1, wherein step (a) is performed prior to step (b), and further comprising the step of:

(c) immersing the medical device in the first solution comprising an organic solvent and a multifunctional crosslinking agent subsequent to immersing the medical device in the second solution.

5. The method of claim 1, wherein the multifunctional crosslinking agent comprises a *bis*-variant of polyethylene glycol, polyethylene oxide, or polyethylene glycol.

6. The method of claim 1, wherein the cross-linkable biomolecule comprises a cross-linkable adsorbable biomolecule.

7. The method of claim 6, wherein the cross-linkable adsorbable biomolecule comprises a cross-linkable adsorbable heparin activity biomolecule.

8. A method of forming a thromboresistant coating on a porous surface of a medical device, comprising the ordered steps of:

(a) providing a medical device with a porous surface;

(b) wetting the porous surface by immersion in a wetting solution;

(c) immersing the porous surface in a first solution comprising a first organic solvent and a multifunctional crosslinking agent;

(d) immersing the porous surface in a second solution comprising a second organic solvent and a cross-linkable biomolecule; and

(e) immersing the porous surface in the first solution comprising the first organic solvent and the multifunctional crosslinking agent.

9. The method of claim 8, wherein the porous surface comprises expanded polytetrafluoroethylene.

10. The method of claim 8, wherein the wetting solution comprises an organic solvent.

11. The method of claim 10, wherein the organic solvent comprises acetone, isopropanol, acetonitrile, methanol, ethanol or a combination thereof.

12. The method of claim 8, wherein the multifunctional crosslinking agent comprises a *bis*-variant of polyethylene glycol, polyethylene oxide, or polyethylene glycol.

13. The method of claim 12, wherein the *bis*-variant of polyethylene glycol, polyethylene oxide, or polyethylene glycol is bis-(benzotriazole carbonate) polyethylene glycol.

14. The method of claim 12, wherein the *bis*-variant of polyethylene glycol, polyethylene oxide, or polyethylene glycol is at a concentration between about 0.001 mg/mL and 500 mg/mL.

15. The method of claim 12, wherein the *bis*-variant of polyethylene glycol, polyethylene oxide, or polyethylene glycol is at a concentration between about 0.2 mg/mL and 10 mg/mL.

16. The method of claim 12, wherein the first organic solvent is acetonitrile or acetone, and wherein the first solution does not comprise water.

17. The method of claim 8, wherein the first solution does not comprise water and the second solution comprises from about 10 to 80 percent water by volume.

18. The method of claim 8, wherein the cross-linkable biomolecule comprises a cross-linkable adsorbable biomolecule.

19. The method of claim 18, wherein the cross-linkable adsorbable biomolecule comprises a conjugate of at least one prosthetic hydrophobic unit and a heparin activity biomolecule.

20. The method of claim 19, wherein the conjugate of at least one prosthetic hydrophobic unit and a heparin activity biomolecule is from 1 to 30 hydrophobic silyl moieties conjugated to the heparin activity biomolecule.

21. The method of claim 20, wherein the conjugate of from 1 to 30 hydrophobic silyl moieties and the heparin activity biomolecule is at a concentration in the second solution of from about 0.01% to about 10%.

22. The method of claim 20, wherein the conjugate of from 1 to 30 hydrophobic silyl moieties and the heparin activity biomolecule is at a concentration in the second solution of from about .25% to about 1.5%.

23. The method of claim 20, wherein the conjugate of from 1 to 30 hydrophobic silyl moieties and the heparin activity biomolecule is benzyl-*bis*(dimethylsilylmethyl)$_x$-oxycarbamoyl-heparin.

24. The method of claim 20, wherein the second organic solvent is the same as the first organic solvent.

25. The method of claim 24, wherein the second solution further comprises from about 10 to 80 percent water by volume.

26. The method of claim 8, wherein immersing in each step is for between about 5 minutes and two hours.

27. The method of claim 26, wherein immersing the porous surface in the first solution is in each step for between about 15 minutes and about one hour.

28. The method of claim 26, wherein immersing the porous surface in the second solution is for between about 45 minutes and about 75 minutes.

29. A thromboresistant expanded polytetrafluoroethylene vascular graft comprising:

a tubular expanded polytetrafluoroethylene construct with an interior lumen; and

a cross-linked co-polymer coating on the surface of the interior lumen, the cross-linked co-polymer coating consisting essentially of a conjugate of at least one prosthetic hydrophobic unit and a heparin activity biomolecule cross-linked with a *bis*-variant of polyethylene glycol, polyethylene oxide, or polyethylene glycol.

30. The graft of claim 29, wherein the conjugate of at least one prosthetic hydrophobic unit and a heparin activity biomolecule is from 1 to 30 hydrophobic silyl moieties conjugated to the heparin activity biomolecule.

31. The graft of claim 29, wherein the *bis*-variant of polyethylene glycol, polyethylene oxide, or polyethylene glycol is bis-(benzotriazole carbonate) polyethylene glycol.

32. A medical device with a thromboresistant blood-contacting surface, comprising:

a medical device with at least one porous blood-contacting surface; and

a cross-linked co-polymer coating on the porous surface, the cross-linked co-polymer coating consisting essentially of a conjugate of at least one prosthetic hydrophobic unit and a heparin activity biomolecule cross-linked with a *bis*-variant of polyethylene glycol, polyethylene oxide, or polyethylene glycol.

33. The medical device of claim 32, wherein the at least one porous blood-contacting surface comprises expanded polytetrafluoroethylene.

34. The medical device of claim 32, wherein the at least one porous blood-contacting surface comprises a woven polymeric surface.

35. The medical device of claim 32, wherein the conjugate of at least one prosthetic hydrophobic unit and a heparin activity biomolecule is from 1 to 30 hydrophobic silyl moieties conjugated to the heparin activity biomolecule.

36. The graft of claim 32, wherein the *bis*-variant of polyethylene glycol, polyethylene oxide, or polyethylene glycol is bis-(benzotriazole carbonate) polyethylene glycol.

37. A thromboresistant coating for a medical device, comprising an in situ cross-linked co-polymer consisting essentially of a conjugate of at least one prosthetic hydrophobic unit and a heparin activity biomolecule cross-linked with a *bis*-variant of polyethylene glycol, polyethylene oxide, or polyethylene glycol.

38. The coating of claim 37, wherein the conjugate of at least one prosthetic hydrophobic unit and a heparin activity biomolecule is from 1 to 30 hydrophobic silyl moieties conjugated to the heparin activity biomolecule.

39. The coating of claim 37, wherein the *bis*-variant of polyethylene glycol, polyethylene oxide, or polyethylene glycol is bis-(benzotriazole carbonate) polyethylene glycol.